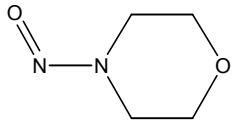
N-NITROSOMORPHOLINE
CAS No. 59-89-2
First Listed in the *Second Annual Report on Carcinogens*



CARCINOGENICITY

N-Nitrosomorpholine is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.17, 1978; IARC S.7, 1987; Lijinsky et al., 1988). When administered in the drinking water, *N*-nitrosomorpholine induced hepatocellular carcinomas, cystadenomas, cholangiofibromas, cholangiocarcinomas, and hemangiosarcomas of the liver, neoplasms of the tongue and esophagus, and epithelial kidney tumors in rats and benign hepatocellular neoplasms and lung adenomas in male mice. When administered by subcutaneous injection, *N*-nitrosomorpholine induced lung adenomas, neoplasms of the trachea, and nasal cavity squamous cell papillomas and carcinomas, anaplastic carcinomas, adenocarcinomas, olfactory neuroepitheliomas, and epidermoid carcinomas in hamsters of both sexes. When administered by intravenous injection, this chemical induced hepatocellular carcinomas and carcinomas of the ethmoturbinals in rats. When added to the water of tanks, *N*-nitrosomorpholine induced liver neoplasms in fish.

There are no data available to evaluate the carcinogenicity of *N*-nitrosomorpholine in humans.

PROPERTIES

N-Nitrosomorpholine is a yellow crystalline solid. It is miscible in water and soluble in organic solvents and is sensitive to light. When heated to decomposition, it emits toxic fumes of nitrogen oxides (NO_x). It is oxidized by strong oxidants to corresponding nitramine. It can be reduced to the corresponding hydrazine and/or amine. It is resistant to hydrolysis.

USE

There is no evidence that *N*-nitrosomorpholine is used commercially in the United States, although patents have been issued for its use as a solvent for polyacrylonitrile and as an intermediate in the production of *N*-aminomorpholine. It was found to be effective as an antimicrobial agent, but there is no evidence that it is used in this manner (IARC V.17, 1978).

PRODUCTION

The Chem Sources USA directory identified two producers and six suppliers of *N*-nitrosomorpholine in 1986 (Chem Sources, 1986). Synthetic production of nitrosamines is limited to small quantities, produced primarily for research (HEEP, 1980). No production, import, or export data were available.

EXPOSURE

The primary routes of potential human exposure to *N*-nitrosomorpholine are inhalation, ingestion, and dermal contact. It has high mobility in soil. It photolyzes rapidly (half-life in sunlight is 30 minutes). Workers in chemical research laboratories and in the rubber and tire manufacturing industry may possibly be exposed to the chemical. An average worker in a rubber or tire factory may possibly be exposed to amounts ranging from 9 to 130 µg of *N*-nitrosomorpholine per day. Wastewater from such factories has been found to contain *N*-nitrosomorpholine; dirt scrapings from a staircase in one factory revealed a *N*-nitrosomorpholine concentration of 730 µg/g, and a soil sample taken outside this plant contained 4.4 µg/g. Investigators have detected *N*-nitrosomorpholine as a contaminant in analytical-grade dichloromethane, chloroform, morpholine (0.8 µg/g), and a rubber cross-linked accelerator (0.4-0.7 µg/g) (IARC V.17, 1978). *N*-Nitrosamines are frequently produced during rubber processing and may be present as contaminants in the final rubber products. Potential exposure depends on the ability of the nitrosamines to migrate from the product and enter the body. CPSC and FDA determined that the nitrosamines present in pacifiers and baby bottle nipples can migrate from the pacifier or nipple into saliva, which could result in ingestion of nitrosamines. Significant levels of *N*-nitroso compounds have been identified in a number of materials including pesticides, cosmetics, cutting fluids, and fire resistant hydraulic fluids. The *N*-nitroso compounds found in these products were apparently formed in situ during storage or handling as the result of a reaction between amines present in the mixture and inorganic nitrite, which may have been added as a corrosion inhibitor. Consumer exposure may occur through ingestion of contaminated products. *N*-Nitroso compounds have been identified in a variety of vegetables, fruits, cheeses, meats, and alcoholic beverages (CHIP, 1978). It is present in snuff in the range of 24-690 ppb (Brunnemann et al., 1982).

REGULATIONS

EPA regulates *N*-nitrosomorpholine under the Resource Conservation and Recovery Act (RCRA) and Superfund Amendments and Reauthorization Act (SARA), subjecting it to reporting/recordkeeping requirements. EPA solicited comments on designating a reportable quantity (RQ) for *N*-nitrosomorpholine under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). OSHA regulates *N*-nitrosomorpholine under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-108.